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DESIGN CRITERIA

FOR

MICROBIOLOGICAL FACILITIES

FORT DETRICK, MARYLAND

VOLUME I INTRODUCTION

U.S. ARMY BIOLOGICAL LABORATORIES

FORT DETRICK, FREDERICK, MARYLAND

DESIGN CRITERIA

FOR

MICROBIOLOGICAL FACILITIES

AT

FORT DETRICK

VOLUME I INTRODUCTION

Prepared for
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by

ASSOCIATED ENGINEERS & CONSULTANTS, INC.

Garden City, N. Y.

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FOREWORD

This is Volume I of a two-volume Manual of Design Criteria, based mainly on biological safety considerations. Volume II, which has been prepared for the use of architect-engineers in designing new or modified microbiological facilities for Fort Detrick, is divided into six sections, each of which is addressed to the specialist in a given field of engineering and design. A brief Table of Contents for Volume II is included in this volume.

As indicated by its title, Volume I provides an introduction for the specialized users of Volume II. However, it is a self-contained document that is intended primarily for the use of readers with an overall viewpoint, such as management personnel at Fort Detrick or their counterparts, who may be concerned with the broad planning of microbiological facilities. For this reason it is bound separately from Volume II. Volume I includes a discussion of safety philosophy, and some representative construction cost data; for the users of Volume II it contains also a brief description of Fort Detrick basic principles of design.

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VOLUME I

INTRODUCTION TO DESIGN

CRITERIA FOR MICROBIOLOGICAL FACILITIES

This volume is divided into two parts, each intended for a somewhat different audience. Part A has a broad aim; it is addressed to management personnel responsible for planning, budgeting, and making policy decisions for the construction or remodelling of microbiological research laboratories. Part B is specifically concerned with basic principles of design of a microbiological facility and its supporting services. Part B serves as an introduction to Volume II, the manual of detailed design criteria based on biological safety considerations that has been prepared for the use of architect-engineers in designing new or modified facilities for Fort Detrick.

PART A. FOR THE MANAGER

In designing and equipping a microbiological research laboratory for the study of diseases infectious for man and animals, it is necessary to provide protection for the experimenter, the experiment, and the surrounding community. The U. S. Army Biological Laboratories often act as a consultant in such design. In our experience, the most conspicuous error in planning is failure to make all the necessary policy decisions before design is begun. This failure results in protective or percautionary features that are excessive, inadequate, incompatible, or inconsistent. The following information is intended to assist those making such decisions. It includes a discussion of safety philosophy and of a number of questions that may arise in applying it, and some representative construction cost data and "rule-of-thumb" estimating factors.

I. MICROBIOLOGICAL SAFETY DESIGN PHILOSOPHY *

In designing microbiological research laboratories, the following safety objectives may be listed:

1. To protect the experimenter and his co-workers against exposure to infectious or toxic materials.

2. To protect the surrounding community against the escape of infectious microorganisms or toxic products that can cause illness in man or domestic animals or damage to crops.

* Much of the material in this section is taken from a paper by A. G. Wedum and G. B. Phillips.

3. To protect the validity of the experiment by avoiding contamination with extraneous microorganisms.

4. To design buildings, equipment, and devices that provide adequate safety, but do not unduly hamper the worker, so that it is more convenient to carry out the work in a safe manner rather than in an unsafe manner.

The specific causes of recorded laboratory infections have been identified in only 35% of our cases, in spite of an intensive review and analysis of each laboratory infection. The high proportion of unidentified causes indicates the need for safety measures that attack the problem on a broad front, by applying all reasonable methods of confining microorganisms within controlled environments.

Basic Approach

Figure 1 illustrates the basic approach in a simplified manner. The boxes enclose isolated areas of different levels of infectious risk. These areas may be suites of rooms, single rooms, or the space within a gastight cabinet. Means must be provided for movement between these zones - movement of men, animals, equipment, air, liquids - without permitting the passage of microorganisms. As indicated by the arrows, movement is directed along a clean-contaminated axis, in the direction of increasing hazard.

The approach outlined in Figure 1 involves the application of the following principles of control:

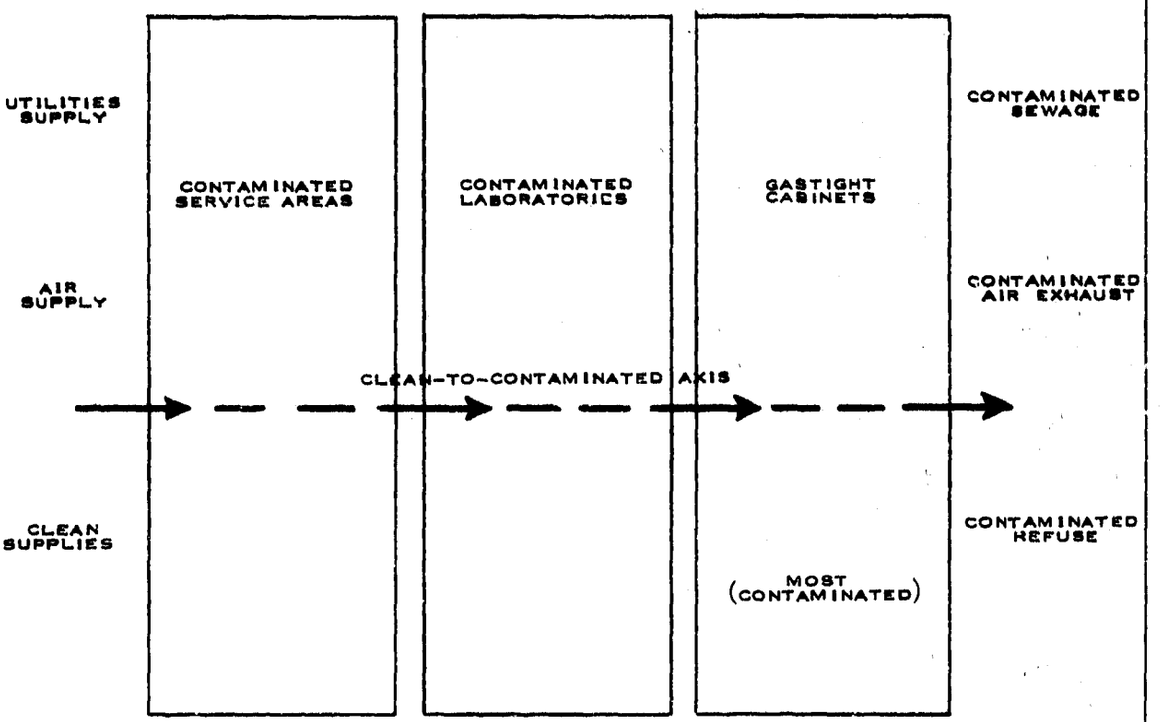
1. The building is divided into contaminated and non-contaminated areas, and the contaminated area is sub-divided into areas of different degrees of contamination.

2. Barriers such as biological safety cabinets, ultraviolet air locks, change rooms, sterilizers, and disinfectant showers are provided between contaminated and non-contaminated areas, and between areas of different degrees of contamination.

3. Ventilation air movement is always from less contaminated to more contaminated areas, and the air is never recirculated. The exhaust air is filtered before discharge to atmosphere.

4. Personnel and materials are decontaminated before leaving contaminated areas.

5. Materials of construction, surface finishes, and design features are selected for ease and effectiveness of decontamination and to provide effective biological barriers.



BASIC APPROACH TO BIOLOGICAL SAFETY DESIGN	FIGURE NO. 1

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Each of these principles leads to its own list of design measures, which are the subject matter of Volume II of this manual. These design measures must be successfully integrated with procedural safeguards, such as personnel training, vaccinations, prescribed laboratory techniques, record keeping, etc., which are outside the scope of a design manual.

Design Problems

For those faced with initiating a design plan the problem is one of determining which, if any, of the various design measures are to be used and to what extent.

Even though a substantial amount of information is available to those planning to construct or remodel infectious disease laboratories, we have been impressed with the difficulties often encountered in design. It is apparent that decisions made in the planning phase all too frequently result in an arrangement that:

1. Provides a degree of inflexible protection for personnel that is excessive in relation to the risk-level of the infectious operations actually to be done, or

2. Provides adequate protection for the experiment but little or none for the experimenter, or

3. Provides excellent microbiological protection for the surrounding community but little for the building occupants, or

4. Provides a degree of protection for personnel that is insufficient when the laboratory gets into full operation.

To avoid these situations, certain questions must be asked and answered before a design is started. Experience in our own laboratories and during consultations and inspections we have been privileged to make at laboratories elsewhere, show that the most conspicuous error in planning a microbiological laboratory is the failure to make all the necessary policy decisions.

The following discussion is directed to the administrator, the microbiological technical consultant, the architect, and the engineer who need these decisions on policy. To some extent, the criteria and ideas set forth may be applied to any laboratory handling hazardous chemicals or toxic substances. The opinions and recommendations in the following pages are based upon visits to many laboratories in this country and abroad, upon thorough investigation of many laboratory-acquired infections, upon probing into the psychological, mechanical, and operational causes of laboratory accidents, and upon assessment under experimental and operational conditions of the value of various protective measures. The following presentation is not intended to encompass all the engineering problems that arise, but to furnish some major examples.

Questions on Policy

Early in the process of designing the laboratory building, policy decisions are necessary beyond the usual ones concerning size, shape, materials of construction, location, personnel capacity, general purpose, etc. These attitional decisions will determine construction details. Some of the questions to be considered and some of the reasons for these questions are:

1. Is this building for the use of a particular senior scientist or for a specific project, and will the building at the departure of the man or conclusion of the project be remodeled to suit the next occupant or next project?

2. To what extent do the views of the laboratory director (or whoever has the final authority to determine the level of precautionary design, equipment, and techniques) reflect the probable view of his eventual successor? This is a sobering thought that sometimes is not considered.

3. How many persons will be at work and what will be the conditions of supervision? The larger the number of nonprofessional personnel, the more desirable it is to provide building design and equipment engineered to insure use of the desired method from which few deviations will occur because it is easier to do it the right (safe) way. Conversely, the smaller the number of persons, the better the judgment based on education and experience, and the closer the supervision of the group, the fewer will be the mechanical safeguards that will be necessary. However, there are some operations in which no amount of judgment and experience can substitute for special equipment.

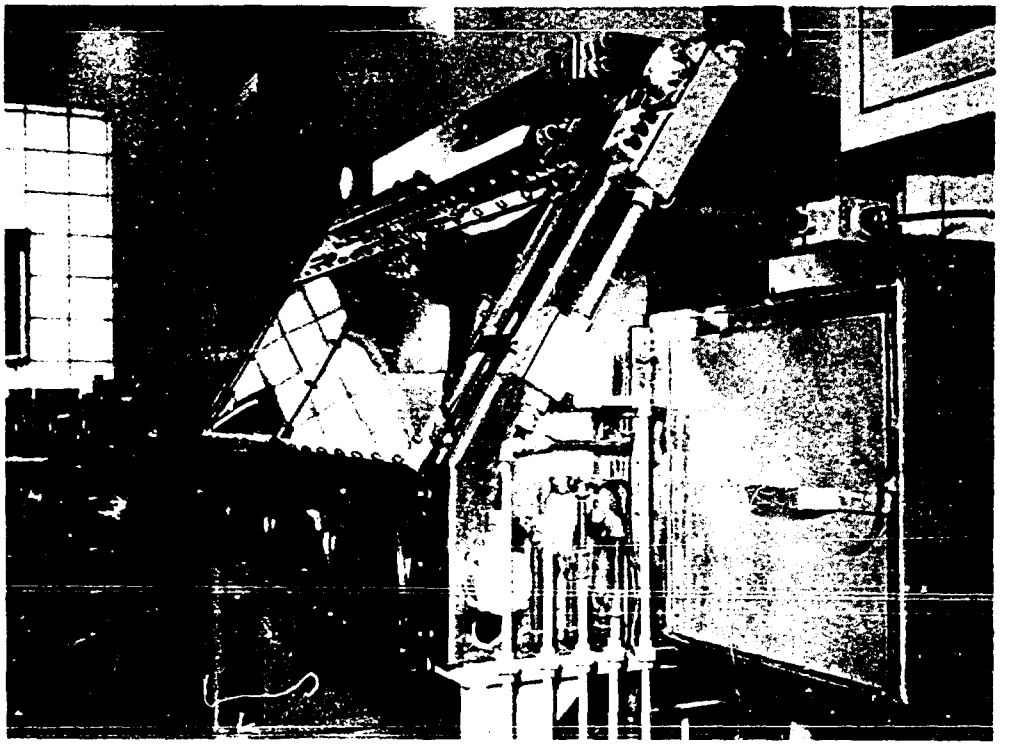
4. What will be the ratio of men to women? The numbers usually are not the same. More flexibility in personnel policy may be facilitated by dividing the total change room space in a 40:60 or 30:70 ratio so that the predominant sex may use the larger room.

5. Does the stated justification and objective of the laboratory require the building to be suitable for study of any infectious microorganism in any type of experiment, with only the size of the equipment or animal as limitation? If so, a gastight cabinet system (Figure 2 or equivalent) will be mandatory for some operations.

6. Will infectious microorganisms be studied as aerosols, relative to (a) aerodynamic stability; (b) particle size; (c) mechanisms of accidental dissemination; (d) animal infectivity evaluations, temperature, humidity, and aerial chemical disinfectants; and (e) other types of investigations? Special airtight chambers and an associated gastight cabinet system are required for many agents.

7. Will any limitations be placed upon the type of etiologic agent that may be studied? Categories of agents, and examples of associated

Array of Gastight Safety Cabinets | Figure 2



Individual Safety Cabinet,
Front Closed, U.V. Pass-Box on Right | Figure 3

recommended requirements for equipment are outlined in Table 1 and in the next section headed "Estimation of Risk".

8. What methods of animal inoculation will be permissible?

(a) Respiratory challenge: Whole-body exposure, head only, nose and mouth only? For these techniques, a protective cabinet and other housing (Figures 2 and 3, and Table 1) are essential for the aerosol apparatus and the animals. Each step in the handling of animals and cages must be carefully considered. Pressure-tight ducts should conduct exhaust air from the site of aerosol liberation to a filter. If the volume of aerosol and concentration of agent is high, the filter should be followed by an air incinerator. Absence of pressure-tight exhaust lines is inconsistent with precautionary air filtration or air sterilization by incineration. With some organisms, use of masks on immunized personnel will permit certain types of work on an open laboratory bench, but we advise that this expedient be avoided.

(b) Intranasal, intratracheal, intraperitoneal, intravenous, subcutaneous, intramuscular, intracerebral, oral, etc.? If personnel are vaccinated, it may be possible to perform injections on an open bench top, but the range of permissible operations and agents is extended by presence of a protective cabinet (Table 1).

9. Which of the following animals will be used: mouse, rat, hamster, guinea pig, ferret, monkey, chimpanzee, fowl, cat, dog?

Animal caging arrangements must be examined for the possibility that cross-infection between animals may impair the integrity of the experiments. Whether this will happen depends upon the agent, the animal, and the method of inoculation.

When infected animals the size of monkeys or smaller are to be housed, thought should be given as to how the animals are to be isolated. The best isolation is that obtained with individually ventilated, closed cages with small inlet and outlet air filters. Ventilated cage racks are suitable in many instances. The possibility of using open cages on ultraviolet-irradiated racks, or non-ventilated filter-top cages, should not be overlooked. Permanently mounted cages have the disadvantage that dependence must be put on chemical sterilization. When infectious organisms are combined with animal excreta, bedding, and other matter, chemicals are not reliable for all microorganisms. Usually, portable stainless steel cages that can be moved to an autoclave or other adequate sterilizing equipment are the most desirable, although disposable or autoclavable plastic cages are useful in some instances.

If the larger animals have been exposed to infectious aerosols, obtaining temperatures, blood samples, etc. is difficult unless they are kept in an open room or in open-front cages, with or without ultraviolet

Table 1

Correlation of Estimation of Risk
with Recommendations for Protective Cabinets [a]

Disease or Agent	Cabinet System[c] Aerosol Studies	Single Cabinets[d] Aerosol Studies	Single Cabinets[d] Other Techniques
Brucellosis	+++		+++
Coccidioidomycosis	+++		+++
Russian s-s encephalitis	+++		+++
Tuberculosis	+++		+++
Monkey B virus	+++		++
Glanders	++	+++	+++
Melioidosis	++	+++	+++
Rift Valley fever	++	+++	+++
Encephalitides, various		+++	++
Psittacosis	++	+++	++
Rocky Mt. spotted fever	++	+++	++
Q fever	++	+++	++
Typhus	++	+++	++
Tularemia	++	+++	++
Tularemia[b]		++	+
Venezuelan encephalitis[b]		+++	+
Anthrax	+++		±
Botulism[b]	++	+++	±
Histoplasmosis		+++	±
Leptospirosis		+++	±
Plague	+++		±
Poliomelitis	+++		±
Rabies	+++		±
Smallpox[b]	+++		±
Typhoid		+++	0
Adeno, entero, viruses		++	±
Diphtheria[b]		++	0
Fungi, various		++	0
Influenza		+	±
Meningococcus		++	0
Pneumococcus		++	0
Streptococcus		++	0
Tetanus[b]		++	0
Vaccinia[b]		++	0
Yellow fever[b]		++	0
Salmonellosis		+	±
Shigellosis		+	±
Infectious hepatitis			±
Newcastle virus		+	0

a. +++ = mandatory; ++ = strongly advised; + = optional, but in absence of a cabinet a few infections will occur; ± = depending upon technique and supervision. 0 = not required.
b. For persons receiving live vaccine or toxoid.
c. Figure 2 or equivalent.
d. Figure 3 or equivalent.

irradiation; or in a special room in which personnel are protected by ventilated suits, ventilated head hoods served by air lines, gas masks, or respirators. Gas masks and respirators are not advised for daily routine use as the primary barrier to human infection because of (a) difficulty in maintaining a good fit on the face, (b) respiratory difficulty experienced by some persons, (c) maintenance troubles, and (d) the practice of occasionally moving the mask or respirator "to get a good breath of air". Masks and respirators should be reserved for the purpose for which they were designed, namely, emergencies and short-term special occasions. In such a room all ceiling and wall openings for air ducts, electrical wall switches, light, water, etc. should be sealed pressure tight to prevent air-borne organisms' entering the basement, attic, or adjoining rooms. Light fixtures inset flush with the ceiling are unsuitable if they permit air to pass into the attic. Placing light switches outside the room is a good idea. To maintain an infection-free attic, exhaust air ducts serving the animal room should be pressure tight, thereby minimizing the dependence on the inward direction of any air leakage through duct joints. A disinfectant shower-airlock entryway to the room may be warranted.

Hair and dander in animal rooms create problems with air ducts and bacterial filters. Prefilters are advised. Even with prefilters there may be filter-loading problems in a room housing chickens. Prefilters should be located in the animal room where they may be changed <u>easily</u> by laboratory personnel. This situation typifies a difficult engineering problem of how to maintain air balance when filters serving different building areas load at different rates.

Year-around climatic control in the animal-holding area is important. It is easier to achieve in the absence of windows.

Dead animals should be incinerated. It is safest and most convenient to do this in an incinerator constructed in the same building as the animal room. This incinerator also may handle other combustible trash. Otherwise, there is a safety and materials handling problem that requires packaging and preliminary autoclaving before transportation to an outside central incinerator, or transportation in a closed, disposable leakproof bag by a trained crew. A study of comparative costs is suggested. Size and design of the incinerator require very careful study, with special attention to the local building code, the largest expected cadaver, and the amount of plastics to be burned, as well as the effect of the incinerator on the building ventilation.

10. Will animals as large as swine, sheep, burros, or calves be used? Rooms for them require good drainage. Flushing-type drains are preferable because of the volume of excreta.

11. What will be the usual physical form of the infectious material - wet or dry? Dry infectious materials aerosolize more easily than wet and therefore are more dangerous. Maximum precautions are necessary.

12. Will infected arthropods be grown and studied in transmission experiments? Will any of these arthropods be exotic to the geographic area of the laboratory? If so, additional air locks with fine mesh screen are desirable. Walls should be smooth, with high-gloss white paint to facilitate detection of escaped insects. Incoming utility lines should be sealed around the point of entrance to the room. Exotic vectors require careful control even if uninfected because of their potential ability to set up a heretofore unknown cycle of transmission of disease.

13. Will there be work with several tissue culture cell lines used to grow viruses? A special room or enclosure with filtered air may be necessary. Positive air pressure in a room may be requested for uninfected tissue cultures if no "clean" space is provided outside the infectious unit.

14. Will large numbers of eggs be used as culture material? Will egg contents be pooled, and into what volume? Egg trays are difficult to sterilize except by autoclaving. Eggs externally contaminated during inoculation require special precautions during handling, incubation, and subsequent processing. If infection of man has a serious outcome, it is best to have the egg incubator sealed to and part of the gastight cabinet where the eggs are inoculated.

15. Is it desirable to be able to change the size, shape, and purpose of the rooms and their installed equipment from time to time? A common finding is that the space needed for animals is underestimated, but the reverse also occurs. Planning for alternative use as laboratory or animal room may be worthwhile. At Fort Detrick, our experience with laboratory-acquired illness has caused us to increase installation of gastight cabinet systems, replacing the single cabinets to some extent. Less dangerous agents are examined and less dangerous techniques are performed in the single cabinets, of which there is a considerable variety (Figure 3). Nonhazardous agents or easily controlled operations are done on the open laboratory bench top. A summary of minimum recommended requirements is shown in Table 1.

The space allotted the engineers for mechanical equipment serving the building utilities often is grossly inadequate. Likewise, the attic and/or basement should be 7 to 10 feet high to permit access for workmen installing or changing air ducts, service lines, filters, and motors. Motors and blowers produce less objectionable noise if they are placed outside the laboratory. Nonengineering personnel unacquainted with a building of this kind find it difficult to understand the need for this amount of space. Sometimes it must be seen to be believed. The attic becomes very crowded and needs mechanical ventilation. It should be sealed pressure tight from the potentially infectious areas below. Likewise, if potentially contaminated pipes or ducts run through the basement, there should be a concrete floor with drains. If ducts and utility lines are placed in wall chases or above corridor false ceilings, these spaces should be designed to permit changes in the ducts and lines. To reduce risk during maintenance, as much engineering service equipment as possible should be in the "clean" area.

16. Will the nature of the experiments, or the species of animals used, or significant change in type of agent and experiment, or resident microbial contamination in the room endangering validity of experiment and product, or nonspecific animal infection such as epidemic diarrhea of mice, or potential infection of personnel, or periodic repair or modification by engineering personnel, make it desirable that all, or some, rooms, air ducts, air filter plenums, and air filters be sterilized periodically by gas such as betapropiolactone or steam-formaldehyde? If so, attention must be given to air-tightness of walls, ceilings, light fixture, air duct and utility insertions, windows, if any, and sometimes even the electrical conduit and electrical switches. These precautions also will assist in controlling condensation and vermin. False ceilings are undesirable in laboratories and animal rooms. If perforated false ceilings are used in the corridors, there may be large unsealed openings in the barrier wall above the false ceiling, between the "clean" and "contaminated" parts of the building. These openings should be made pressure tight. The air ducts are not suitable conveyors for decontaminating gases; condensation occurs at angles and bends, which causes maldistribution and rusting. Instead, a portable decontaminating apparatus is positioned in the open room, from which gas enters the air ducts if this is desired. All surface finishes must be evaluated for chemical resistance to decontaminating agents.

17. Will shaking machines holding microbial cultures be operated in walk-in incubators or refrigerators? In case of breakage of flasks on the shakers there is needed (a) a light switch, an ultraviolet light switch, and a power switch for the shaker, all located outside the incubator or refrigerator; (b) a view glass in the door for observation before entrance; (c) an ultraviolet fixture inside the incubator or refrigerator to reduce airborne microbial contamination before entrance after an accident. (In a laboratory, the 10 to 12 air changes per hour will be an effective substitute.)

18. Will any of the experiments result in animal excreta, the uncontrolled disposal of which would endanger domestic, farm, or feral animals? Examples: anthrax, glanders, equine encephalitides. In general, it must be presumed that all excreta from experimental animals is infective until proved otherwise. Are there any other reasons of law, public relations, volume of material, or microbial virulence that make disinfection or sterilization of sewage necessary?

It is well to check this matter in advance with the local civil officials. Infectious disease units handling only small animals, amounts of cultures in test tubes and flasks, and infectious agents characteristic of a hospital or diagnostic laboratory ordinarily do not need to decontaminate sewage. The autoclaving of infected cages and debris and the sterilization of cultures before discard assures that few if any infectious organisms are discharged in the liquid wastes.

However, if the sewage is to be decontaminated, this commonly is done by steam in a retention tank in the basement or outside the building.

The tank should be in an enclosure (which could be in the open air without a roof) with concrete floor and walls high enough to hold all the contents in case of leakage. A recording thermometer and easily accessible control panel for convenient daily observation and adjustment is desirable. If spores are not a consideration, pasteurization may be sufficient (200°F for 30 seconds). Where sterility is needed, our tests show that 260°F for about ten minutes will be effective. Whether batch sterilization in a tank or continuous flow through heated pipes is used, depends upon an engineering economic evaluation.

19. What is the personnel policy regarding occupational health?

(a) As a condition of employment, must employees accept vaccination with commercial standard vaccines and with experimental vaccines when, in the opinion of the laboratory director, administration of these would decrease the chance of clinically apparent illness? A "yes" answer will reduce the need for mechanical protection, if only those agents are studied for which a vaccine is available.

(b) What level of occupational infection is acceptable to management? Subclinical infection detectable only serologically? Minor discomfort no more than from a reactive avirulent living vaccine, which causes only a minority to cease work for one to three days? A "no" answer to these questions may make the difference between installation of individual protective cabinets (Figure 3) and installation of much more expensive gastight systems (Figure 2), depending again upon the agent and the experiments.

20. For public relations, economic, legal or other reasons, to what extent is protection from infection of persons <u>not</u> working in this laboratory considered to be of comparatively great importance?

Often a building that amply protects the surrounding community with such arrangements as air locks, change rooms, filtration or incineration of exhaust air, special treatment of sewage, and ultraviolet barriers, does not provide the building occupants themselves with a corresponding degree of protection. For instance, only chemical fume hoods are installed, or no protective ventilated microbiological work cabinets are provided, or those installed are only three feet wide. This size is recommended as suitable only for very limited and specilized operations on a small scale, typically in a general laboratory characterized by absence of air locks, change rooms, etc. Often these three-foot units become merely display items, not connected to the air exhaust system, rarely used for the good reason that they are too small for routine work. In a laboratory constructed primarily for work with highly infectious agents, cabinets need to be constructed, equipped, and placed so that they are the most convenient place to work. This assumes that work with truly hazardous agents is underway. When not so used, the glass door panel can be raised and the cabinet used as if it were a laboratory bench top. In the absence of such cabinets, conscious or unconscious choices are made to avoid

hazardous agents. Sometimes use of a nonpathogenic simulant is rationalized as being adequate to study the "basic mechanisms of action" of the pathogen. It is the experience of our laboratories that this rationalization often is unwarranted. In any event, nonpathogens can, and should, be studied in less expensive surroundings. Another likely discrepancy is the absence of an autoclave or a satisfactory equivalent to sterilize animal cages before cage litter is removed, prior to cleaning, or, if present, the autoclave is not convenient to the animal rooms. Both of these conditions encourage human infection. Often, no provision is made to prevent animal-to-animal cross infection, and presumably, in such instances for some diseases, animal-to-man transmission.

The reason for disproportionate emphasis on microbiological safety often lies principally with the resident microbiologists who act as consultants during design. There is an understandable human tendency to approve or tolerate arrangements that require little change in working habits, such as passage through a clothing change room and shower, clean laboratory clothing, air handling, and sewage decontamination. Objection most likely arises when the working site at the laboratory bench is affected by proposals for protective cabinets and enclosures of various kinds. Unfortunately, operations at the laboratory bench or animal cage within a few inches of the worker's nose are the source of most human infections. All other protective features are secondary in importance as far as safety of the employee is concerned.

Of course, this disproportionate emphasis is completely justified if the diseases to be studied will be limited to those that are not dangerous for man but would be a serious threat to domestic animals if they escaped from the laboratory. A few examples are: African swine fever, African horse sickness, lumpy skin disease, and blue tongue of sheep and cattle.

21. What are the local zoning laws and building codes relative to an infectious laboratory? What changes in these laws and codes can be foreseen? In what direction are they moving as concerns disposal of potentially infectious wastes and noncombustible trash?

22. Is study contemplated, now or in the future, of diseases for which permission, and in some cases inspection, may be required by the U.S. Department of Agriculture and/or the U.S. Public Health Service? Examples: Rift Valley fever and African swine fever. We are informed that increase in importation of infectious agents and their vectors, and the increased number of laboratories handling infectious agents, has caused USDA and USPHS to plan for closer examination of imports and laboratories handling them. Both government agencies will give great weight to the competence and integrity of the scientist as well as to the quantity of material being handled in determining whether or not a laboratory is suitable under their regulations. Since there are no clear-cut criteria, if there is any plan to handle highly infectious material it is strongly suggested that the responsible government agencies be consulted regarding the plans before commitment for construction is made.

23. Will any equipment, significantly contaminated by an infectious microorganism or toxin, need to be sent periodically to the manufacturer for repair or adjustment, or need to be repaired or adjusted by his service men? If so, some arrangement for decontamination of this apparatus may be desirable. For delicate apparatus, ethylene oxide gas is very useful. For economy, it must be used in a leakproof space such as a suitably modified autoclave.

24. In the geographical area concerned, are there sufficient dusts, bacterial spores, fungi, molds, or insects so that intake air should pass through a filter? Our experience is that such filtration is desirable. The air supply fan should shut off automatically if the exhaust fan for a contaminated area accidentally stops, to prevent pressurizing the contaminated area. However, the exhaust fan should not cut off automatically when the intake fan stops. An alternate but less certain method of controlling nonspecific microbial contamination is to provide ultraviolet ceiling fixtures, to be turned on overnight.

25. Where will the experimental animals be obtained? Unless the effort is relatively small, it is better for animals to be produced and prepared apart from the area of research, to avoid complicating accidental infection. A "clean" area where animals can be quarantined for a suitable time before use is helpful.

26. As part of a periodic cleaning or disinfection process will it be necessary to flood the floors? If so, special attention must be given to prevent cracks, not only around floor or sink drains but also anywhere else. Apparently it is very difficult to make a concrete floor that will not crack and permit seepage of water into the room below.

27. How reliable is the source of power for the building? The major danger to employees is an air flow stoppage in a protective ventilated cabinet during a hazardous experiment with aerosolized microorganisms. Perishable refrigerated materials usually can be transferred to a cooler that uses solid carbon dioxide. Contaminated sewage is no problem if personnel leave the building and the retention sewage tank is large enough for batch chemical sterilization. Inasmuch as work stops, exhaust air is of no concern. However, animals in closed, mechanically ventilated cages will die in about an hour if there is no ventilation. For this reason, the extent of use of ventilated cages will be a factor in evaluating the need for standby auxiliary power.

28. Are the animals in each experiment held for only a short time, e.g. 30 days or less, or are they to be held for a long time, e.g. a year or more as in some research on chronic diseases, leukemia, or cancer? In the latter case in which the animals may present little risk to man, the animals need protection from diseases transmissible to them by the animal caretaker, and from naturally occurring epidemic animal disease either latent in some of the experimental animals or introducible from nearby other animals.

Estimation of Risk

To assist in answering some of the questions concerning policy and to provide a basis for making other decisions and accepting or rejecting some of the suggestions outlined above and in Table 1, the following "Estimation of Risk" is offered for consideration:

As a guideline, the following orders of decreasing magnitude of risk and decreasing complexity of precautionary measures are proposed for diseases of man and animals as studied in the laboratory. The emphasis upon aerosol dissemination derives from the belief that future research will make increasing use of aerosol challenge in the study of respiratory diseases.

1. Suitable for any type of experiment with any microorganism and any animal up to the size of a chimpanzee.

2. Preparation of dry powders of infectious agents.

3. Dissemination of pathogenic microbial aerosols.

(a) Organisms highly infectious for man, producing a distressing disease for which there is an incompletely protective vaccine and only partially successful specific chemotherapy. The difficulty in treating such syndromes as pneumonic plague causes their aerosolized pathogenic agents to be included at this level of hazard, even though they are not as readily infective as some others.

(b) Organisms infectious for man, producing disease that is incapacitating but usually not serious when acquired in the laboratory, for which there is an incompletely protective vaccine and no specific chemotherapy. Although the glanders organism is less infective and the disease may be treated with sulfadiazine, it should be included here because of the dangerous clinical syndrome produced.

(c) Toxins or organisms highly infectious for man, producing disease for which there is either effective vaccination and/or effective specific chemotherapy.

4. Laboratory studies not involving planned dissemination of aerosols. The subclassification would be the same as in 3 above.

5. Dissemination of dry or fluid aerosols of organisms with comparatively low invasiveness, usually with no vaccine available, often subject to specific chemotherapeusis, but sometimes causing serious pneumonia, such as staphylococcus, streptococcus, and pneumococcus.

6. Laboratory studies not involving dry powders or planned dissemination of aerosols, with organisms of less serious risk because of various mitigating factors present to varying degrees, such as availability of vaccination, specific treatment, and low infectivity in the laboratory.

7. Minor infections.

(a) Nuisance diseases such as Newcastle virus conjunctivitis.

(b) Organisms seldom causing laboratory infection such as pneumococcus, streptococcus, staphylococcus, meningococcus, vaccinia virus, and diphtheria and tetanus bacilli.

8. Classroom demonstrations or student work with killed, stained preparations or with attenuated strains.

Comment

The most common source of laboratory-acquired infection is the inhalation of accidentally or experimentally created microbial aerosol. Therefore, control of air is very important. Control should begin where the aerosol is formed. To the extent that this is achieved, other features such as differential air pressures in rooms, protective respiratory equipment, ultraviolet irradiation, and personnel showers become less important in protecting the employee.

When air from a chamber or cabinet where microbial aerosols arise is filtered or incinerated, then filtration of air from the open room and building becomes less critical. Incineration ordinarily is limited to air exhausted from aerosol vessels and from gastight cabinet systems.

Separate air-handling systems for the non-contaminated area, the contaminated area, and the animal room area are useful when the size of the building permits. These may facilitate the flow of air from the less hazardous areas to the more hazardous. Recirculating air systems may be used in the non-contaminated office area if this is a separate system. The effectiveness of ultraviolet air locks between such areas has been tested and proved. To illustrate the efficiency of air pressure differentials, a difference of 0.1 of an inch of water pressure at 70°F will result in an air velocity flow of 1266 linear feet per minute. Even a pressure difference as low as 0.001 of an inch of water will result in a flow of 126 linear feet per minute.

II. CONSTRUCTION COSTS

Table 2 lists the construction costs of 10 infectious disease research laboratories built at Fort Detrick between 1951 and 1957. These buildings varied greatly in size and function, so it is not surprising to find a considerable range in cost per square foot, from $33 to $63 without installed or portable equipment, and from $42 to $77 per square foot with such equipment. Pieces of equipment costing less than $200 and the cost of land are not included.

When these costs are adjusted to a basis of June, 1965, using the ENR Building Cost Index for Baltimore (see Figure 4), the range becomes $41 to

Table 2

Cost Analysis of Ten Infectious Disease Research Laboratory Buildings at Fort Detrick Built Between 1951 and 1957

Building	Date	Gross Area, ft^2	Building Cost			Original Cost, $/ft^2$ (gross)		Adjusted Cost+, $/ft^2$ (gross)	
			Construction	Equipment*	Total	Space Only	Space plus Equipment	Space Only	Space plus Equipment
376	5-53	35,508	$2,234,000	$ 495,673	$2,729,673	$62.92	$76.87	$87.40	$106.80
467	5-53	12,507	502,274	30,656	532,930	40.16	42.61	55.90	59.30
468	5-53	38,326	1,433,853	456,147	1,890,000	37.41	49.31	52.00	68.50
469	11-52	5,236	250,189	35,892	286,081	47.78	54.64	67.60	77.40
539	7-55	116,878	4,291,118	742,311	5,033,429	36.71	43.07	46.40	54.60
550	8-53	19,885	854,285	296,261	1,150,546	42.96	57.86	59.30	79.90
560	11-55	170,155	5,565,168	1,582,684	7,147,852	32.71	42.01	40.60	52.10
567	5-51	33,084	1,641,662	621,669	2,263,331	49.62	68.41	70.50	97.10
568	9-53	49,278	2,193,431	396,705	2,590,136	44.51	52.56	61.20	72.30
1412	8-57	69,978	3,725,857	1,439,916	5,165,773	53.24	73.82	61.30	84.90
Simple Average		55,084	2,269,184	609,791	2,878,975	44.80	56.12	60.20	75.30
Weighted Average		-	-	-	-	41.20	52.30	53.10	67.50

* Includes installed and portable equipment; excludes pieces costing less than $200.

+ Adjusted to June 1965 using ENR Building Cost Index for Baltimore.

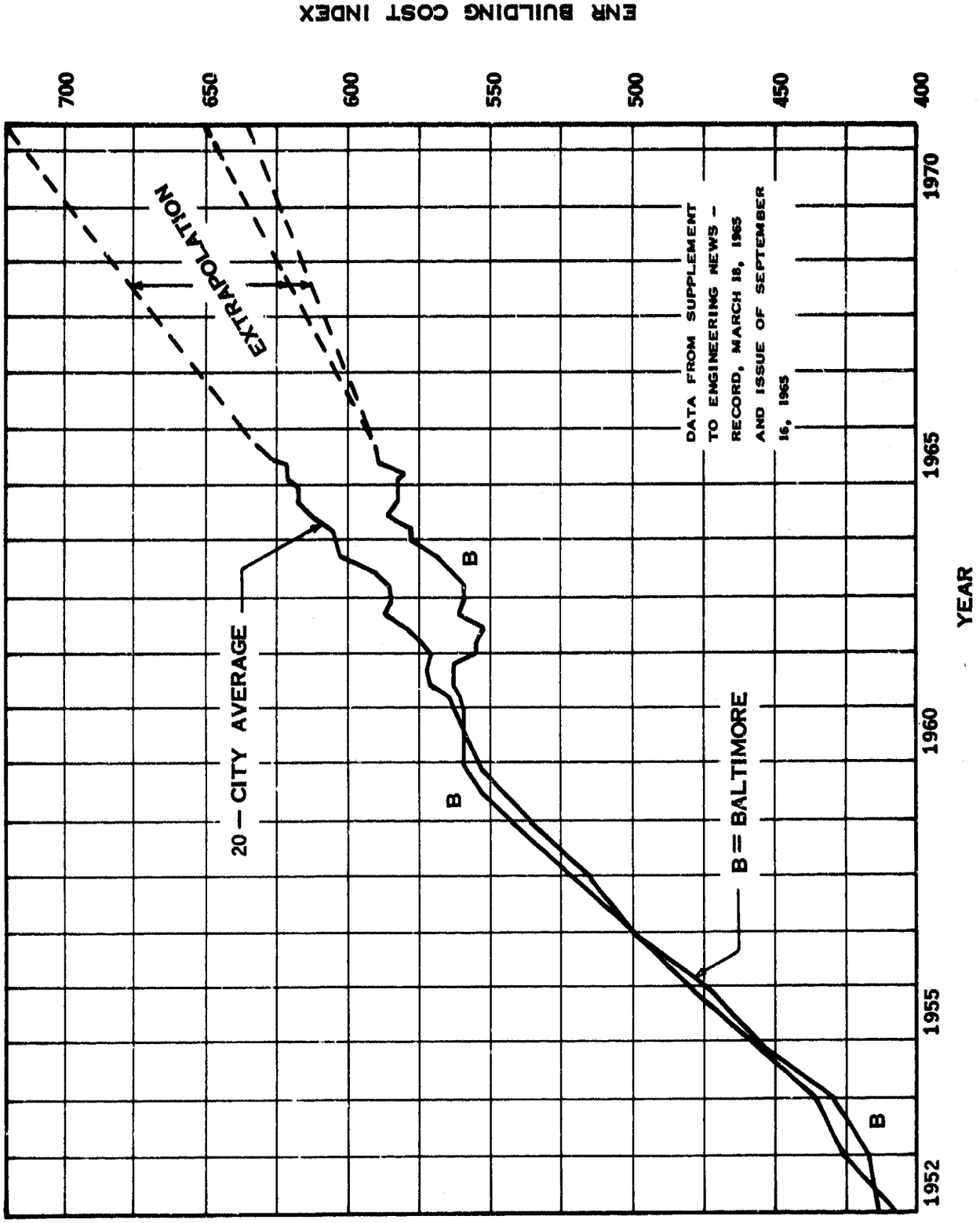


Figure 4. Building Cost Index, 1952-1965

$87 per square foot without equipment, and $52 to $107 per square foot with equipment.

The above costs are based on the gross building floor space, which includes the basement and the floored portion of any part of the attic that has at least 5 feet of headroom. Measurements are outside dimensions, and the space occupied by walls and partitions, pipe chases, elevator shafts, and the like are included. Analysis of the space breakdown for these 10 buildings indicates the following average distribution:

65% is available for direct and indirect labor use (net floor space):

- 24% - laboratory space
- 19% - direct support space such as glassware washing, incubator, refrigeration, animal rooms, greenhouses, preparations, etc.

43% "working space"

- 22% - secondary support, such as change rooms, corridors, offices storage space, conference rooms, etc.

35% is attic and basement space.

Note that of any major area, walls and partitions will reduce the actual available space by about 15%.

It should be noted that the space breakdown varies considerably from building to building, and the costs given above should therefore be used only for orientation and preliminary budget estimates.

It should also be realized that the cost of building maintenance is much higher than for some other types of facility. For example, at Fort Detrick, maintenance costs per square foot for laboratory buildings are almost twice that for family housing and more than four times that for warehouses. The average annual maintenance cost for laboratory buildings at Fort Detrick in 1964 was $0.30 per square foot of gross area. It is recommended that provision be made so that these costs are not charged to the budget for animals, scientific equipment, and laboratory supplies, lest it bear the burden of maintenance costs to the detriment of the research effort.

Another factor that is often underestimated in planning microbiological laboratories is the water requirement. This may easily vary by an order of magnitude from one building to another, but a rough average figure is 1 gallon per day per square foot of building area (this does not include cooling water required for air conditioning equipment). Closely related to this figure is the amount of contaminated liquid waste to be handled, which may run from one-fourth to three-fourths of the water consumption.

PART B. FOR THE ARCHITECT-ENGINEER

The remainder of this volume is intended to provide an introduction and background information for the users of Volume II. The manual of safety design criteria contained in Volume II has been prepared for the guidance of architect-engineers in designing microbiological facilities at Fort Detrick. Its purpose is to present primarily the special design criteria, based on biological safety considerations, that must be met to protect the worker, the work, and the surrounding community. The effectiveness of such protection depends both on design features and operating procedures. Operating procedures are outside the scope of the manual and they have been referred to only where this was necessary for a clear presentation of the design criteria.

The manual is not intended to duplicate the fund of standards and criteria normally possessed by the architect-engineer. However, some information on Fort Detrick Design Practices not related to safety is included, and Appendix A (Vol. II) lists a number of Fort Detrick Purchase Descriptions and Specifications that are available. Finally, the Guide Specifications and Engineering Manual of the Corps of Engineers, Department of the Army, are to be used in the design and preparation of plans and specifications to the extent applicable.

Volume II is divided into six sections, corresponding to the normal division of design work in an engineering office. Each section is addressed to the specialist in a given field and is largely self-contained, so that he may employ it without having to read the other sections (except as directed to them by cross-reference). The brief Table of Contents at the front of this volume gives a general indication of the scope of Volume II, and the individual Table of Contents at the front of each Section in Volume II outlines the scope in considerable detail.

While Volume I serves as an introduction and source of site utility information for users of Volume II, the latter is the complete and exclusive source of design criteria. Any criteria appearing in Volume I are for illustration only.

The following pages give a general description of the utilities and services available on a post-wide basis, and a short list of factors pertinent to design and construction at Fort Detrick. This information is intended primarily for orientation, and more detailed information of this type will be supplied to the individual architect-engineer as required, or should be solicited by him. A final section discusses briefly the changes in safety philosophy at Fort Detrick over the years.

I. GENERAL UTILITIES AND SERVICES

1. Postwide Services: There are a number of utilities and services that are of a postwide nature and are available to the various buildings.

These include contaminated sewage, sanitary sewage, storm drains, cold water, 110 psig steam, condensate return, electric power, telephone, and an alarm system.

a. Contaminated Waste Treatment Plant: All laboratory and experimental facilities generating liquid biological wastes are connected into the contaminated sewage system, which consists of buried lines from 4" to 12" in diameter, encased in concrete for identification and protection. This system carries waste to the central continuous waste treatment plant where it is held in large tanks prior to heat sterilization, cooling, and release to the sanitary sewage system.

b. Sanitary Swewage: All buildings on the post are connected into a single sanitary sewage system. In buildings in which biologically contaminated wastes are generated, segregation of the building into contaminated and non-contaminated sections with corresponding drain systems permits discharge of wastes to the proper sewage system. The sanitary sewage treatment plant is located offsite on the Monocacy River, at a distance of 3 miles.

c. Storm Drains: Storm drains collecting runoff of rain water are collected in a separate system and discharged into Carroll Creek.

d. Refuse Incinerator: A post refuse incinerator for refuse from non-contaminated buildings is located at the sanitary sewage treatment plant. Trash, rubbish, and sterilized carcasses of experimental animals from contaminated buildings are taken to an incinerator located within the restricted area.

e. Waste Air Incinerator: The exhaust air from certain sources of relatively high hazard, including Class III biological safety cabinets, process equipment, aerosol chambers, waste collection treatment tanks among others, is incinerated before discharge to the atmosphere. In some cases this is done in small electrically heated incinerators located in the various buildings. In other cases, where the volume to be handled and other conditions make it desirable, the contaminated exhaust (CVI) from a group of buildings is manifolded and brought to a large externally located combustion incinerator, which operates at 550°F (at the stack base). There are four such large incinerators on the post.

f. Water Supply: A single 75 psig water supply system is used to supply cold water to all buildings for drinking, sanitary, and experimental use. The water purification plant is located on the Monocacy River upstream of the sanitary sewage treatment plant. Provision is made so that the water plant can be tied into the Frederick water system on a reciprocal basis. The purification treatment consists of pre-chlorination, flocculation, sedimentation, sand filtration, and post-chlorination. Within each laboratory or experimental building a separate break tank is used to segregate the water supply being used in the contaminated portion of the building. Hot water is provided locally in each building.

g. 110 Psig Steam: A central steam plant supplies 110 psig steam to all biological laboratory buildings on the post. Steam is also used in laboratory and experimental facilities as a sterilization medium and is tapped off the building supply and reduced in pressure to meet the requirements of the equipment.

h. Condensate Return: Steam used for building heating purposes is returned to the central steam plant through the condensate return system. However, steam used for sterilization or process use is discharged to the contaminated sewage system to prevent any possibility of contaminating the steam or condensate systems.

i. Electric Power: Electric power is supplied by the Potomac Edison Co. at 34.5 kilovolts, 3-phase, 3-wire, 60-cycle, delta. A 4.16 kilovolt, 3-phase, 4-wire wye grounded distribution system runs throughout the post and provides electrical power for all facilities.

j. Telephone: A post-wide telephone system is connected to each building on the base providing local as well as long distance telephone service.

k. Alarm System: A post-wide alarm system is provided throughout the base which may signal off-normal operations of various types. This system is connected to a central annunciator in the waste collection treatment plant.

2. Common Services: The following services are sometimes supplied by a common system to a group of related buildings:

Propane gas
Nitrogen
Cooling tower water

II. FACTORS AFFECTING ARCHITECT-ENGINEERS

Biological safety considerations impose certain restrictions on architect-engineers which they should be aware of in planning their work. If their personnel require access to microbiological facilities in normal use, they probably will have to be vaccinated. This usually will involve a series of injections; in some cases access may be permissible immediately after the first injection, in others a delay of several weeks may be involved. Generally the injections are administered at Fort Detrick, but where this will impose a considerable added travel expense, the possibility of arranging for injections by the architect-engineer's physician should be investigated. Whenever possible, facility inspection should be planned for periods when the building has been decontaminated, either for the annual maintenance shut-down, which occurs at different times and lasts for several weeks, or for other shut-downs.

Such considerations are more significant in the case of construction

contractor personnel. The architect-engineer will need to take these into consideration in preparing bid documents, and to a minor extent in preparing construction cost estimates. In this category it may be noted that final tie-in of new work to existing "contaminated" waste lines is done by Government forces.

There are security requirements to be met, which in general will not be burdensome. Most of the work is perfomed on an unclassified basis. Visitors' badges are issued by local authority, and visits should have advance authorization. The microbiological facilities are within a separately fenced area, to which appropriate access with escort is arranged as required.

III. CHANGES IN SAFETY PHILOSOPHY

Construction of microbiological facilities at Fort Detrick started in 1943, and reached a peak in the early nineteen fifties. Early designs were based on the limited experience available from related fields. Over the years safety philosophy has undergone modifications on the basis of accummulated experience, research in safety methods, and the introduction of new materials and equipment. This process has been accompanied by a continually improving safety record.

The changes in safety philosophy have been changes in emphasis rather than principle. Primary emphasis is placed on preventing the release of microorganisms from the laboratory working surface, which has led to increased use of primary containment devices such as ventilated safety cabinets. To the extent that the microbiological hazards are controlled at their source, other building features, such as differential air pressures in rooms, protective respiratory equipment, ultraviolet irradiation, and personnel showers become less important in protecting laboratory employees. However, all of these features are still extensively used, because they play an important part in protecting the surrounding community, especially in case of accidental release of infectious material.

Consequently, while the changes in safety philosophy have been reflected in changes in design criteria as new buildings were added, these have not been drastic. Nevertheless, they must be taken into consideration when additions or modifications are made to existing facilities, which is frequently the case. Apparent contradictions may easily arise, and the architect-engineer will have to exercise flexibility and judgment in applying the criteria. Guidance will be provided by the Contract Scope of Work insofar as the issues can be foreseen, and additional help will be given by the Contract Officer as new ones come to light during the design period.

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ON

MICROBIOLOGICAL LABORATORY DESIGN

CONTENTS

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13. ABSTRACT

This is Volume I of a two-volume Manual of Design Criteria for Microbiological Facilities, based mainly on biological safety considerations.

Volume I provides an introduction to the subject matter both for managers and the specialized users of Volume II. The volume includes a discussion of safety philosophy and some representative construction cost data slanted primarily toward management needs. It also includes a brief description of basic microbiological facility design principles aimed primarily at the architect and engineer. A selected bibliography of the literature on microbiological laboratory design concludes the volume.

Volume II is prepared for the use of architects and engineers in designing new or modified microbiological facilities for Fort Detrick. It is divided into six sections, corresponding to the normal division of design work: architectural; heating, ventilation, and air-conditioning; piping; equipment and accessories; electrical; and instrumentation and controls. Each section is designed to be largely self-contained for the use of the individual specialists involved. A detailed Table of Contents, an alphabetical Subject Index, numerous illustrative plates, a glossary, and supporting appendices also are included.

The information in these two volumes supercede that in AD 265 957, Technical Requirements for the Design of Bacteriological Facilities, 1 May 1961, which is outdated and should no longer be used.

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